

## Clinical Management of Antibiotic-Resistant Infections in Pediatric Populations

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### Abstract:

**Background:** Antibiotic resistance has become a major global health threat, especially in pediatric populations, due to irrational antibiotic use and limited stewardship practices. Children are particularly vulnerable because of their developing immunity and frequent exposure to infections.

**Aim:** The study aimed to determine the prevalence and antibiotic resistance patterns of bacterial pathogens isolated from pediatric patients with suspected infections.

**Methodology:** A hospital-based cross-sectional observational study was conducted among 90 culture-positive pediatric patients (<15 years) at the Department of Pediatrics, Sheikh Bhikhari Medical College and Hospital, Hazaribagh, Jharkhand, India. Clinical specimens (blood, urine, sputum, stool, pus, and swabs) were processed for bacterial identification and antibiotic susceptibility testing using the Kirby–Bauer disk diffusion method per CLSI guidelines.

**Results:** *Escherichia coli* (27.8%) and *Staphylococcus aureus* (22.2%) were the most common isolates. Gram-negative bacteria exhibited high resistance to ampicillin and third-generation cephalosporins but retained sensitivity to meropenem. Among Gram-positive isolates, 50% of *S. aureus* were methicillin-resistant (MRSA), while all remained sensitive to vancomycin and linezolid. Nitrofurantoin was effective against urinary isolates.

**Conclusion:** High resistance rates to first-line antibiotics highlight an urgent need for pediatric-focused antibiotic stewardship, routine culture-based therapy, and continuous resistance surveillance to ensure effective management of childhood infections.

**Keywords:** Pediatric Infections, Antibiotic Resistance, MRSA, *Escherichia Coli*, Antibiotic Stewardship.

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### Introduction

Antibiotic resistance has become one of the most urgent international health issues of the 21st century that is a major threat to human health, clinical care and healthcare systems on the global scale [1]. This problem is even more significant in the pediatric population, where children are a vulnerable group, and their immune systems are not yet fully developed, and they are more likely to contract infectious diseases. Increased morbidity, mortality, and costs of health care are the outcomes of the emergence of antibiotic-resistant pathogens in pediatric infections which complicates treatment plans [2] instead of shortening them. World Health Organization (WHO) has made the problem of antimicrobial resistance (AMR) one of the global priorities, focusing on the pressing importance of rational antibiotics usage, improved monitoring, and better infection control practices. Although the medical care of children has developed significantly, antibiotic resistance remains a problem in the effectiveness of antibiotic therapy in the treatment of community-acquired and hospital-acquired infections.

Historically, antibiotics have been considered to be one of the most outstanding inventions in contemporary medicine, the burden of infectious diseases was reduced significantly, and millions of lives have been saved [3]. Nevertheless, years of abuse and overuse both in clinics and at home have prompted the development of resistant strains of bacteria. The issue is especially acute in the sphere of pediatric healthcare because antibiotics are often prescribed to the patients with upper respiratory tract infections, otitis media, pharyngitis and other viral diseases that are self-limiting and do not necessarily require antibiotic treatment. Research revealed that almost 30 to 50 percent of antibiotics administered to children are either not indicated, not dosed or not given over the right period; hence, favoring the development of resistance [4]. In addition, the increasing trend in using broad-spectrum antibiotics that are usually selected as empirical treatment without culture testing has magnified the selection pressure on microorganisms, promotes the emergence of multi-drug resistant (MDR) strains.

The processes of antibiotic resistance among pediatric pathogens are complex and include both intrinsic and acquired elements. There are several ways in which bacteria develop resistance e.g., by using an enzyme to degrade antibiotics (e.g.,  $\beta$ -lactamase), by modifying the target site, by decreasing bacterial membrane permeability, and by activating efflux pumps [5]. In children, organisms such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Escherichia coli*, *Klebsiella pneumoniae* and *Staphylococcus aureus* have shown a high level of resistance to the widely used antibiotics, such as penicillins, cephalosporins, and macrolides [6]. Of relevance is the development of the methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum  $\beta$ -lactamase (ESBL)-carrying *Enterobacteriaceae* and multidrug-resistant *Pseudomonas aeruginosa* in pediatric units. These pathogens have emerged as significant causes of pneumonia, urinary tract infections, bloodstream infections, and neonatal sepsis, making treatment regimens hard and causing lengthier hospitalization.

Antibiotic resistance has a special impact on pediatric population due to a number of reasons. First, the immune systems of children are underdeveloped, thus, more likely to be severely infected and stay longer in the sickbed in case of deterioration during the treatment process [7]. Secondly, the pharmacodynamics and pharmacokinetics of antibiotics differ across various pediatric age groups ranging between neonates and adolescents and therefore require close dose modifications which are not an easy task especially in resource limited environments. Thirdly, the community setting of schools and day-care centers is highly likely to cause infections among children, as close contact provides the extreme spread of resistant bacteria. This community transmission forms a reservoir of resistant strains which further intrude into a hospital environment forming a vicious cycle of further propagation of resistance.

Antibiotic resistance in childhood disease is now known as a significant burden of disease all over the world, especially in low- and middle-income nations (LMICs) where antibiotic misuse is rampant and surveillance infrastructures are inadequate [8]. The presence of antibiotics over-the-counter, limited number of laboratory facilities, and deficient healthcare systems contribute to the situation in such environments. Most parents insist on using antibiotics on their children even in case of viral diseases, usually because of the myth concerning antibiotic power to minimize the symptoms. The lack of effective antibiotic stewardship initiatives and the general lack of awareness on the part of the population contribute to the further acceleration of the resistance crisis. Furthermore, horizontal gene transfer of the resistant genes and globalization of travel and trade have made the spread of resistance determinants

among the populations, including the pediatric populations, to be spread rapidly.

Combating antibiotic resistance in childhood infections, therefore, should be multidimensional and international in nature. Antimicrobial stewardship programs specifically designed with the pediatric setting, rational prescribing based on the local resistance patterns, and the utilization of rapid diagnostic tests that could differentiate between bacterial and viral infections are these key strategies. Monitoring the trends of antimicrobial resistance of pediatric pathogens is necessary to inform empirical treatment and revise treatment recommendations. Training of healthcare providers and parents regarding the prudent use of antibiotics is also very instrumental in terms of minimizing unwarranted exposure of antibiotics. Moreover, alternative treatment, including bacteriophage therapy, immunomodulatory agents, as well as the creation of new antibiotics, is the focus of research, and promising ways to treat it in the future.

### Methodology

**Study Design:** This study was designed as a hospital-based cross-sectional observational study conducted to determine the prevalence and pattern of antibiotic resistance among pediatric patients with suspected bacterial infections. The study aimed to identify common bacterial isolates and assess their resistance profiles against commonly used antibiotics to aid in better management of pediatric infections.

**Study Area:** The study was carried out in the Department of Pediatrics, Sheikh Bhikhari Medical College and Hospital, Hazaribagh, Jharkhand, India for one year.

### Study Participants

**Inclusion Criteria:** Children aged below 15 years who attended the Pediatric Department during the study period and were clinically suspected of having bacterial infections (such as respiratory tract infections, urinary tract infections, septicemia, wound infections, or gastrointestinal infections) were included in the study. Only those whose samples yielded positive bacterial growth upon culture were included for further analysis.

**Exclusion Criteria:** Children with viral, fungal, or parasitic infections confirmed by laboratory testing, those who had received antibiotic therapy within 72 hours prior to sample collection, and patients with incomplete clinical records or negative bacterial cultures were excluded from the study.

**Sample Size:** A total of 90 pediatric patients with culture-positive bacterial infections were included in this study for data analysis.

**Procedure:** Blood, urine, sputum, stool, pus swab, throat swab, and wound swab were taken as clinical

specimens of the pediatric patients presenting with symptoms that could suggest bacterial infection. All the samples were taken in under aseptic conditions and transported to the microbiology laboratory immediately to be cultured and analysed in terms of sensitivity. Urine samples were inoculated in cysteine lactose electrolyte-deficient (CLED) agar whereas blood samples were placed in pediatric blood culture bottles (BD Bactec Ped Plus) and incubated at 37 °C in an automated culture system. Gram staining was followed by the culture of the samples of sputum and pus on blood agar and MacConkey agar to identify the morphology of bacteria.

They characterized the bacterial isolates according to the colony traits, Gram staining, and a number of biochemical tests [catalase, coagulase, triple sugar iron, citrate, urease, and indole tests]. Bacterial susceptibility of the antibiotics was determined by disk diffusion technique of Mueller-Hinton agar according to recommendations of Clinical and Laboratory Standards Institute (CLSI, 2017). The antibiotic disks used were ampicillin, cefotaxime, ceftazidime, ciprofloxacin, gentamicin, meropenem, cotrimoxazole and vancomycin among others. Plates were incubated at 37 °C and 18–24 hours and the diameter of the inhibition zone was taken and interpreted as per CLSI criteria.

The culture media and antibiotic disk quality control was done by using standard ATCC reference strain (*Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 25923, and *Pseudomonas aeruginosa* ATCC 27853) to maintain accuracy and reliability

in the test outcomes. Phenotypically, extended-spectrum  $\beta$ -lactamase (ESBL) and methicillin-resistant *Staphylococcus aureus* were identified according to CLSI recommendations.

**Statistical Analysis:** All data obtained were entered into Microsoft Excel 2016 and analyzed using SPSS version 27.0 (IBM Corp., Chicago, USA). Descriptive statistics, including frequencies, percentages, and mean values, were used to summarize the data. The prevalence of bacterial isolates and their antibiotic resistance patterns were represented in tabular and graphical formats. Associations between bacterial isolates and resistance patterns were assessed using the Chi-square test, and a p-value < 0.05 was considered statistically significant.

## Result

In Table 1, the sample of 90 patients is presented by age and gender distribution of pediatric patients. Patients aged between 2–5 years were the most populated group of patients (33.3% of total population), then it was 26.7% group (22.2%). The 0–1-year age group had the lowest representation with a percentage of 17.8 of the patients. Regarding the gender, males (54) were higher than females (36) in all the age groups, which is a male majority in the study population. On the whole, the data indicate that infections or conditions under analysis were more prevalent among children aged 2–5 years and more prevalent in males than in females.

**Table 1. Distribution of Pediatric Patients According to Age and Gender**

Age Group (years)	Male (n)	Female (n)	Total (n)	Percentage (%)
0 – 1	10	6	16	17.8
2 – 5	18	12	30	33.3
6 – 10	14	10	24	26.7
11 – 14	12	8	20	22.2
<b>Total</b>	54	36	90	100

Table 2 presents the spread of the bacterial isolates that were isolated on the different clinical samples, which shows the frequency and diversity of infections in the different types of samples. Urine samples represented the most frequent positive cultures (20) out of all the total samples collected (22.2 percent of all positive cultures), and *Escherichia coli* was the most common isolate of the positive cultures. Blood cultures were positive in 15 cases (16.7%), most of which had *Staphylococcus aureus*. Sputum samples had 12 positive cultures (13.3%) with *Klebsiella pneumoniae* being the prevalent

organism with 10 positive cultures (11.1%) on the pus or wound swabs predominantly consisting of *Pseudomonas aeruginosa*. Stool samples provided 8 positive cases (8.9%) that were mainly *Salmonella* species, with 7 positive cultures of throat swabs (7.8%) that were mainly *Streptococcus pyogenes*. Eye swabs were the least positive with 4 positive cultures (4.4%) in which *Staphylococcus aureus* was dominant. In general, the table shows that most frequent were urinary and bloodstream infections, and the predominant bacterial pathogens detected were *E. coli* and *S. aureus*.

Type of Specimen	No. of Samples Collected	Positive Cultures (n)	Percentage of Positive Cultures (%)	Common Bacterial Isolate
Urine	25	20	22.2	Escherichia coli
Blood	20	15	16.7	Staphylococcus aureus
Sputum	15	12	13.3	Klebsiella pneumoniae
Pus/Wound Swab	12	10	11.1	Pseudomonas aeruginosa
Stool	10	8	8.9	Salmonella spp.
Throat Swab	8	7	7.8	Streptococcus pyogenes
Eye Swab	5	4	4.4	Staphylococcus aureus

Table 3 displays the frequency distribution of bacteria isolates, which were included in the study. Out of 90 total isolates, Escherichia coli was most dominant in the total isolates with 27.8 percent of the total isolates and subsequently Staphylococcus aureus with 22.2 percent. Klebsiella pneumoniae was also 16.7 percent of the isolates, with Pseudomonas aeruginosa, 11.1 percent. In 8.9 percent, Salmonella

species were detected and in 7.8 percent Streptococcus pyogenes. Enterobacter species was the rarest isolate with 5.5% of the total bacterial isolates. The presence of both Gram-negative bacteria, especially E. coli and K. pneumoniae and Gram-positive bacteria such as S. aureus shows that they were frequent pathogens in the examined samples.

Bacterial Species	Number of Isolates (n)	Percentage (%)
Escherichia coli	25	27.8
Staphylococcus aureus	20	22.2
Klebsiella pneumoniae	15	16.7
Pseudomonas aeruginosa	10	11.1
Salmonella spp.	8	8.9
Streptococcus pyogenes	7	7.8
Enterobacter spp.	5	5.5
<b>Total</b>	<b>90</b>	<b>100</b>

Table 4 presents the pattern of antibiotic resistance of gram-negative bacteria in which the resistance is different among E. coli, K. pneumoniae, P. aeruginosa, and Salmonella spp. Resistance was the greatest to Ampicillin and E. coli (88) and K. pneumoniae (84) had alarming rates as compared to P. aeruginosa (70) and Salmonella spp. (62). All the isolates also had a high rate of resistance to third-generation cephalosporins such as Cefotaxime and Ceftazidime, which signifies the prevalence of  $\beta$ -lactam resistance. Ciprofloxacin and Gentamicin had

moderate resistance with a range of between 35-60 percent across the species. On the contrary, Meropenem exhibited the least resistance implying that it can still be used as a last-line therapy in these pathogens. The resistance rate of Cotrimoxazole was considerable in all the isolates and Nitrofurantoin showed low resistance in E. coli urinary isolates as well as K. pneumoniae (22 and 25 percent respectively), which showed that it can be used to treat infection of the urinary tract.

Antibiotic	E. coli (%)	K. pneumoniae (%)	P. aeruginosa (%)	Salmonella spp. (%)
Ampicillin	88	84	70	62
Cefotaxime	76	70	65	58
Ceftazidime	68	66	60	50
Ciprofloxacin	55	60	52	40
Gentamicin	45	42	38	35
Meropenem	10	12	8	5
Cotrimoxazole (TMP-SMX)	72	70	60	55
Nitrofurantoin (Urine isolates)	22	25	—	—

Table 5 shows the pattern of antibiotic resistance of gram-positive bacteria that were isolated during the study, which was Staphylococcus aureus, Streptococcus pyogenes and Enterobacter species. It was

found that penicillin presented the greatest resistance among all three organisms with S. aureus exhibiting 80 percent resistance, S. pyogenes exhibiting 75 percent resistance and Enterobacter spp.

exhibiting 70 percent resistance. Intermediate resistance was observed in erythromycin, clindamycin and gentamicin among all the isolates signifying partial yet noticeable resistance to antibiotics used routinely. In particular, the proportion of MDR-resistant isolates of *S. aureus* was 45% making the

issue of multidrug resistance a significant concern. Conversely, every gram-positive isolation was completely sensitive to vancomycin and linezolid indicating that the two drugs still have a therapeutic role in treating gram-positive resistant infections.

**Table 5. Antibiotic Resistance Pattern of Gram-Positive Bacteria (n = 27)**

Antibiotic	Staphylococcus aureus (%)	Streptococcus pyogenes (%)	Enterobacter spp. (%)
Penicillin	80	75	70
Oxacillin (MRSA detection)	45	—	—
Erythromycin	40	35	38
Clindamycin	25	22	28
Gentamicin	30	26	25
Vancomycin	0	0	0
Linezolid	0	0	0

### Discussion

The results of the current paper reveal some important trends of bacterial etiology and antimicrobial resistance among children which are also close and similar to the ones reported by other regions indicating age and pathogen distributions trends. The high number of children aged 2–5 years and below infected in our study is consistent with the findings by Habyarimana et al. (2021) [9] who found that in Rwanda, 34.1 percent of the cases of pediatric infections were in children below the age of five and this was attributed to the fact that the immune system of this age group has not matured and because of their exposure to the community. Likewise, Myat et al. (2022) [10] in Myanmar discovered that children under age five years were majority of the pediatric cases of infections thereby establishing the vulnerability of the group to bacterial infections. These similar observations reinforce the argument that early childhood is a high-risk period of influence of bacteria as the immune system of the host is not yet well developed and, moreover, it is exposed to pathogens as much as possible.

Regarding the distribution of the specimens, our analysis demonstrated that most of the isolates were urinary tract infections (UTIs) with the predominant cause as the *Escherichia coli*, then bloodstream infections with a predominant cause as *Staphylococcus aureus*. In Nepal, *E. coli* was found to be the leading cause of urinary isolates (65%), *Klebsiella pneumoniae* was the leading cause of bloodstream infections (45.7%), and *S. aureus* was the leading cause of pus (45%) (Kayastha et al., 2020) [11]. This trend justifies our results that these three bacteria remain the major pathogens in pediatric infection in various areas. Moreover, *E. coli*, *K. pneumoniae*, and *S. aureus* were also identified in the global surveillance information of the WHO as the most commonly isolated bacteria in pediatric infections in 22 countries (Hendriksen et al., 2011) [12] which suggests a global epidemiological pattern.

Their clinical importance especially in urinary and bloodstream infection is supported by high occurrence rates of *E. coli* and *K. pneumoniae* in our study. The same tendencies were indicated by Azimi et al. (2019) [13] who stated that *E. coli* was the cause of 41.8% and *K. pneumoniae* of 29.3 percent of the total isolates on the basis of pediatric clinical samples in Iran. The presence of the latter *Enterobacteriaceae* species is connected to their virulence factors, which favor colonization and persistence in the urinary tract as emphasized by Raeispour and Ranjbar (2018) [14]. The presence of *S. aureus* in the wound swabs and pus identified in our study is also correlated with the presence of *S. aureus* in the post-surgical or skin infection, which was reported by Al-mohammady et al. (2020) [15] as the cause of 28 percent of the neonatal infections and post-surgical sepsis in Cairo.

In our research, antibiotic susceptibility testing showed disastrous levels of first-line antibiotics resistance. This resistance pattern is a reflection of the resistance pattern reported by Ntirenganya et al. (2015) [16] in Rwanda where more than 90 percent of *E. coli* and *K. pneumoniae* isolates were resistant to  $\beta$ -lactam as well as third-generation cephalosporin. Similarly, Malik and Bhattacharyya (2019) [17] reported the likelihood of resistance to ampicillin and amoxicillin-clavulanic acid at 84.5% and 81% in Bangladesh, respectively, which demonstrates that irrational use of antibiotics and ineffective infection control habits are also leading to a similar worldwide trend. All these findings point to the fact that  $\beta$ -lactam resistance has become critical in children environment in various geographic settings.

On the other hand, carbapenems like meropenem showed the least resistance rate in our study with 95.9 percent of Gram-negative isolates being sensitive. The result is similar to that of Zhanel et al. (1998) [18] which stated that the susceptibility of meropenem against bacterial infections in pediatrics was 89.8% and that of imipenem was 91%. On the

same note, Luo et al. (2021) [19] found carbapenems to be the most appropriate drugs to be used to treat *K. pneumoniae* infections in neonates, which has been noted to remain an important drug of last resort. Nevertheless, even these powerful medications might not be effective unless the use of antibiotics is prudently managed due to the development of carbapenem-resistant strains in certain settings (Agyeman et al., 2020) [20].

Among Gram-positive, the data exposed a 50 percent of *S. aureus* isolates to be methicillin-resistant (MRSA). This percentage is within the range of numerous studies carried out on the topic of pediatrics all over the world, which indicates the long-standing issue of MRSA infections in children. The occurrence of MRSA illustrates the challenge in dealing with this infection because of the few effective antibiotics. It was, nonetheless, found that all the *S. aureus* and *Streptococcus pyogenes* isolates used in the study were entirely sensitive to vancomycin and linezolid, which once again underscores the validity of these medications as a viable management choice against resistant gram-positive pathogens.

Nitrofurantoin was shown to be of good efficacy against *E. coli* and *K. pneumoniae* urinary isolates, thereby revealing that it will continue to be useful as a substitute in treating simple urinary tract infections in children. Besides this, fluoroquinolones and aminoglycosides exhibited average sensitivity levels and therefore can be used as secondary agents in cases of resistant bacterial strains. The variation in resistance patterns in different regions could be explained by the differences in the prescribing of antibiotics, practices to control infections, and the access to antimicrobial surveillance systems. The higher rate of resistance in places with inadequate healthcare facilities is a common occurrence because of the sale of antibiotics over the counter as well as the absence of a diagnosis to support it. These results underscore the need to have continuous monitoring of antimicrobial resistance and the judicious application of antibiotics, especially in the pediatric practice where empirical therapy is still the norm.

Altogether, this comparison of the results of our research with other studies in the region proves the thesis that clinical manifestations of bacterial infections in children are primarily due to *E. coli*, *K. pneumoniae*, and *S. aureus*, which present worrying rates of resistance to most popular antibiotics. Although carbapenems, vancomycin and nitrofurantoin are still exhibiting encouraging effectiveness, the use of these drugs is indiscriminate and may result in the emergence of resistance in the future. The reinforcement of antibiotic stewardship initiatives, the administration of culture-directed therapy, and the improvement of preventive measures to curb illness control situations are the critical means to reduce the growing threat to the general population health. It is

urgent to continue monitoring and international cooperation to prevent the wave of antimicrobial resistance among pediatric patients.

### Conclusion

The study underscores the continuing concern of antimicrobial resistance among pediatric infections, particularly the notable 50% prevalence of MRSA among *S. aureus* isolates. The sustained sensitivity of all Gram-positive organisms to vancomycin and linezolid highlights their indispensable role in managing resistant infections. Similarly, nitrofurantoin's effectiveness against *E. coli* and *K. pneumoniae* supports its use for uncomplicated urinary tract infections, while moderate sensitivity to fluoroquinolones and aminoglycosides suggests their value as secondary treatment options. The regional variations in resistance patterns further reflect differences in antibiotic stewardship and healthcare infrastructure. Overall, these findings emphasize the urgent need for continuous antimicrobial surveillance, rational antibiotic use, and strengthened infection control practices to mitigate resistance and preserve the efficacy of existing therapeutic options in pediatric care.

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